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| 10/551,847 | 06/23/2006 | Lin Haixiang | NBMP-001 | 6184 |

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| EXAMINER | |
|---|---|
| LE, EMILY M | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/551,847 | HAIXIANG, LIN | |
| | Examiner | Art Unit | |
| | EMILY M. LE | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09/29/05, 6/23/06, 11/17/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *27-51* is/are pending in the application.

4a) Of the above claim(s) *46-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/07, 12/18/07, 1/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I in the reply filed on 11/17/2008 is acknowledged. The traversal is on the ground(s) that Lin et al. failed to evidence that the shared technical feature failed to provide a contribution over the prior art because the composition of Lin et al. does not teach of a composition having the molecular weight/size defined in the claims. This is not found persuasive because contrary to Applicant's assertion, the composition of Lin et al. does encompass the molecular weight/size recited in the claims. The restriction is based on the claims as originally filed. The original claims require that the polynucleotide adjuvant have a molecular weight in the range of 66,000-1200000 Daltons. Lin et al. teaches of a polynucleotide adjuvant having molecular weight of 5-8S. [Page 309, in particular.] This molecular weight is further collaborated by Applicant. Applicant discloses and established that the polynucleotide adjuvant of Lin et al. has a molecular weight in the range of 38,000-107,000 Daltons. Page 7, Table A of Applicant's specification. The molecular weight of the polynucleotide adjuvant of Lin et al. is within the range required by the original claim.

The requirement is still deemed proper and is therefore made FINAL.

### *Status of Claims*

2. Claims 1-26 are cancelled. Claims 27-51 are added. Claims 46-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely

traversed the restriction (election) requirement in the reply filed on 11/17/2008. Claims 27-45 are under examination.

***Information Disclosure Statement***

3. The information disclosure statements (IDS) submitted on 3/30/07, 12/18/07, and 1/23/08 has been considered. Regarding references that are not written in English, it should be noted that the extent of the information considered is limited to the English summary/abstract Applicant has provided with the foreign references.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is being claimed in the cited claim. As presented, the claim recites only a wherein clause. A preamble, transitional phrase and body of the claim is absent from the claim. For the purpose of examination, claim 30 is interpreted to further limit claim 29.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 27, 29-32 and 34-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Zong et al.,[1] as evidenced by Lin et al.[2]

The claims are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. Claim 27 requires the size to be in the range of 12.8 to 24.0S (Svedbergs). Claims 29-32 require the size to be greater than 9.34S, 12.8S, equal to or greater than 9.3S and equal to or greater than 12.8 S, respectively. Claim 34, which recites dependency to any one of claims 27-33, requires the antibiotic to be kanamycin. Claim 35, which recites dependency to any one of claims 27-33, requires the antibiotic to be kanamycin and the positive ion be calcium. Claim 36, which recites dependency to any one of claims 27-33, requires the antibiotic to be kanamycin and the source of the positive ion be calcium chloride. Claim 37, which recites dependency to any one of claims 27-33, requires the antibiotic to be kanamycin sulfate and the positive ion be provided by calcium chloride.

Zong et al. teaches PICKCa. PICKCa is a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, as evidenced by Lin et al. Lin et al. establishes that PIC is polyriboinosinic-polyribocytidylic acid, K is an antibiotic, and Ca is a positive ion. The antibiotic of PICKCa is kanamycin. The positive

[1] Zong et al. Study on determining the molecular weight of PICKCa and PI,PC with the method of polyacrylamide gel electrophoresis. Chinese Journal of Pharmaceutical Analysis. 1993, Vol. 13, No. 4, pages 219-222. With English abstract, as provided by Applicant on 1/23/2008 IDS.
[2] Lin et al. A new immunostimulatory complex PICKCa in experimental rabies: antiviral and adjvuant effects. Archives of Virology, Vol. 131, Nos: 3-4, September 1993, 307-319. Provided by Applicant on 03/30/2007 IDS.

ion of PICKCa is calcium. The PICKCa of Zong et al. has molecular size ranging from 7.8-13.4S. [Table 2, page 221, in particular.]

In the instant case, the PICKCa of Zong et al. is the same as those claimed. Therefore, Zong et al. anticipates the claimed invention.

Regarding claim 36-37, which requires the positive ion be provided by calcium chloride and the antibiotic be kanamycin sulfate, it should be starting material/source does not further limit the claimed invention, particularly since the source does not impart any structural or functional characteristics on the claimed composition.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 27-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zong et al., in view of Morahan et al. [3] and by Lin et al.,

Claims 28 and 33, which depend on claim 27 and 31, respectively, require the molecular size to about 13.5 to 24.0S and equal to or greater than 13.5S. Claims 38-40 and 43 requires the addition of an antigen to the composition of any one of claims 27, 29-32 and 34-37. Claims 41-42, which is directed at the composition of claims 38-40 and 43, require that the antigen be purified rabies antigen. Claim 44, which is directed

[3] Morahan et al. Antiviral activity and side effects of polyriboinosinic-cytidylic acid complexes as affected by molecular size. Proc. Nat. Acad. Sci., USA, April 1972, Vol. 69, No. 4, 842-846. Provided by Applicant on 12/18/2007 IDS.

at the composition of claims 38-40 and 43, requires that the composition be in solid or liquid form. Claim 45, which is directed tot eh composition of claims 38-40 and 43, requires that the composition be freeze-dried.

Regarding claims 28 and 33, Zong et al. does not teach of a PICKCa having molecular size to about 13.5 to 24.0S and equal to or greater than 13.5S. However, at the time the invention was made, Morahan et al. teaches that the adjuvant activity contributed by PIC correlates with molecular size. Morahan et al. establishes that adjuvant activity increases as molecular size increase. Thus, at the time the invention was made, it would have been prima facie obvious in the art to increase the molecular size of the PICKCa of Zong et al. One of ordinary skill in the art, at the invention was made would have been motivated to do so to optimize the adjuvant activity of PICKCa. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

Regarding claims 38-44, it should be noted that the adjuvant activity of PIC is well known in the art, as established by Morahan et al. Moreover, Lin et al. establishes that PICKCa also has adjuvant activities. Both Morahan et al. and Lin et al. injected a composition comprising said adjuvant with an antigen to induce an immune response in an animal. The antigen that Lin et al. teaches is purified rabies antigen. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to include an antigen with the composition with Zong et al. to produce an injectable PICKCa composition with an antigen, including rabies antigen of Lin et al.

One of ordinary skill in the art, at the time the invention was made would have been motivated to do to produce an injectable immunogenic composition against rabies infection. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because adjuvant activity of PICKCa is well known in the art.

Regarding claim 45, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to freeze-dried/lyophilized the composition. One of ordinary skill in the art, at the time the invention was made would have been motivated to do to stabilize the composition for long term storage. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because freeze-drying or lyophilization is routinely practiced in the art.

Additionally, since the adjuvant activity of PICKCa is well known in the art, PICKCa would inherently enhance the immune response induced by an antigen.

***Double Patenting***

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/331575. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 1 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 1 of the copending patent application also requires the composition be in a sustained release formulation.

In the instant case, the sustained release formulation of the composition of claim 1 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/331839. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 1 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size

specified in the claims. However, claim 1 of the copending patent application also requires the composition be formulated for mucosal administration.

In the instant case, the mucosal formulation of the composition of claim 1 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 of copending Application No. 12/160853. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 9 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 9 of the copending patent application also requires the composition be in a sustained release formulation.

In the instant case, the sustained release formulation of the composition of claim 9 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 27-45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 12/160584. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant patent application are directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims.

Claim 2 of the copending patent application is also directed to a composition comprising polyriboinosinic-polyribocytidylic acid, an antibiotic, and a positive ion, wherein the polyriboinosinic-polyribocytidylic acid has an average molecular size specified in the claims. However, claim 2 of the copending patent application also requires the composition be formulated for mucosal administration.

In the instant case, the mucosal formulation of the composition of claim 2 of the copending patent application is a species of composition claimed in the instant patent application. The species anticipates the genus of composition instantly claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EMILY M LE/
Primary Examiner, Art Unit 1648

/E. M. L./